Biochemo-opto-mechanical (BioCOM) Chip for Chemical and Biomolecular Detection

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Fast, sensitive, inexpensive, and reliable detection of toxic chemicals and biological pathogens is critical for health, environmental, and national security reasons. Conventional methods for pathogen detection [1,2], for example, suffer from at least one of several problems including long analysis time, high instrumentation cost, lack of sensitivity and the inability for real-time monitoring. We introduce a new approach to detecting biomolecules using the biochemo-optomechanical (BioCOM) chip. The technique is based on chemomechanical or thermomechanical actuation of microcantilever beams and optical detection of cantilever deflection using diffractive optics. In essence, our goal is to develop a micromechanical “litmus paper” for color-based detection of biomolecular signatures.

Microcantilever beams are currently used as ultra-sensitive force sensors in many different applications. Figure 1 shows an electron micrograph of a typical microcantilever used in atomic force microscopes (AFMs). Besides their wide use in AFMs where the force is applied at a single point (the tip), microcantilevers have recently been used as sensors for measuring extremely small bending moments that are produced by thermally or chemically generated stresses over the whole cantilever surface. Gimzewski and co-workers [3] at IBM Zurich first showed that a SiN_x/Al bimaterial cantilever beam can be used as a calorimeter to detect the heat of catalytic reaction of H_2 and O_2 on Pt to form H_2O. Thundat et al. [4] also demonstrated the calorimetric use of microcantilevers for detecting enzyme-mediated catalytic biological reactions with femtoJoule resolution. Figure 2 shows a plot of cantilever deflection as a function of glucose concentration when the cantilever surfaces was coated with glucose oxidase. In addition to calorimetry, stresses induced by adsorption or binding of molecules on surfaces can also lead to a bending moment that produces a cantilever deflection. Chen et al. [5] demonstrated that adsorption of Hg on a Au-coated cantilever is sufficiently large to create a measurable deflection. Berger et al. [6] also showed that the adsorption of a self-assembled monolayer of alkane-thiol on a Au surface generated cantilever deflection due to stress that was produced by electrostatic interactions between the functional terminal groups of alkane-thiols. Recently, Thundat and co-workers [4] observed the first Ab-Ag reaction using a cantilever sensor, presumably due to surface stresses generated by intermolecular force interactions of the Ag-Ab complex. Figure 3 shows the measurement using ricin.

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Based on these observations, we are currently developing a chip containing arrays of microcantilever beams that will become a platform for simultaneously detecting a variety of chemicals and biological molecules. Figure 4 shows the design of the BioCOM chip. The chip contains N arrays, each array about 5 mm x 5 mm in size that is visible to the naked eye. Each array contains an array of approximately 50 x 50 microcantilever beams that are each about 100 μm x 100 μm in size. Each of the N arrays is loaded with a single type of molecular species which makes it sensitive to a specific molecule. For example, monoclonal antibodies are attached to the cantilever surface to make it sensitive to a particular antigen. When the BioCOM chip is exposed to an aqueous solution, the high specificity of Ab-Ag or enzyme reaction will chemomechanically or thermomechanical induce deflection of only the particular array of cantilevers. Cantilever deflections can be detected using optical, piezoresistive, or capacitive techniques [7]. However, since biosensing is typically liquid based, optical techniques are more desirable because they do not require electrical contacts to the cantilever. Recently, a novel approach based on diffractive optics of deformable gratings has been introduced to detect deflections of arrays of cantilevers with nanometer resolution with the human eye [8,9]. Figure 5 shows an example of cantilever arrays forming deformable diffraction gratings. This technology is used in the BioCOM chip where each cantilever in the array contains a series of 1-2 μm wide interdigitated fingers. The fingers and the optics have been designed such that incidence of white light on this array of cantilever-based diffraction grating produces a certain color that is visible to the human eye. The BioCOM chip will thus be a micromechanical "litmus paper" for detection of biomolecules.

The attractive features of the BioCOM chip include the following: (i) the chip requires no external power since the actuation is chemomechanical and the detection is based on dispersion of background white light; (ii) the low fabrication and operation costs for the BioCOM chip will make it disposable; (iii) it can be several orders of magnitude more sensitive (parts per trillion levels have been demonstrated for ricin) than existing techniques; (iv) the high specificity of Ag-Ab or enzyme reactions makes the test highly selective; (v) simultaneous detection of N biomolecular species.

References:

1. E. Engvali and P. Perlman, "Enzyme-linked immunosorbent assay (ELISA): Quantative assay of immunoglobulin G," *Immunochemistry* **8**, 871-874 (1971).
2. P. Tijssen, *Practice and Theory of Enzyme Immunoassays*, Elsevier, New York (1985).
3. J. Gimzewski, Ch. Gerber, E. Meyer, R. R. Schlittler, "Observation of a chemical reaction using a micromechanical sensor," *Chem. Phys. Lett.* **217**, 589-594 (1994).
4. T. Thundat, P. I. Oden, R. J. Warmack, "Microcantilever sensors," *Microscale Thermophysical Engr*. **1**, 185-199 (1997).
5. G. Y. Chen, T. Thundat, E. A. Wachter, R. J. Warmack, "Adsorption-induced surface stress and its effects on resonance frequency of microcantilevers," *J. Appl. Phys*. **77**, 3618-3622 (1995).
6. R. Berger, E. Delamarche, H.P. Lang, C. Gerber, J.K. Gimzewski, E. Meyer, H.J. Guntherodt, "Surface stress in the self-assembly of alkanethiols on gold," *Science* **276**, 2021-2024 (1997).
7. D. Sarid, *Scanning Force Microscopy*, Oxford Univ. Press, New York (1994).
8. M. Mao, T. Perazzo, O. Kwon, A. Majumdar, J. Varesi, P. Norton, "Direct-view uncooled micro-optomechanical infrared camera," *Proc. of IEEE-MEMS Conf*., Jan. 17-21, Orlando, pp.100-105 (1999).
9. T. Perazzo, M. Mao, O. Kwon, A. Majumdar, J. Varesi, P. Norton, "Infrared vision using uncooled micro-optomechanical camera," submitted to *Appl. Phys. Lett.*

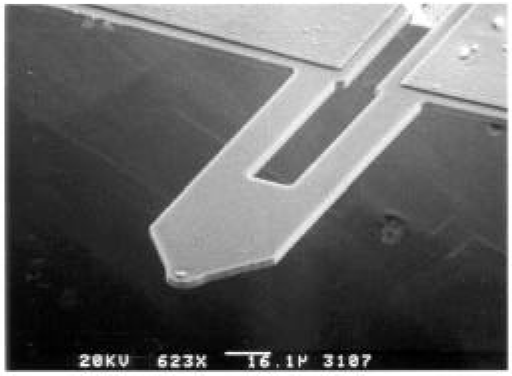

Fig. 1 Electron micrograph of 200-µm long Si microcantilever used for atomic force microscopes. This cantilever uses the piezoresistivity of Si for deflection measurement.

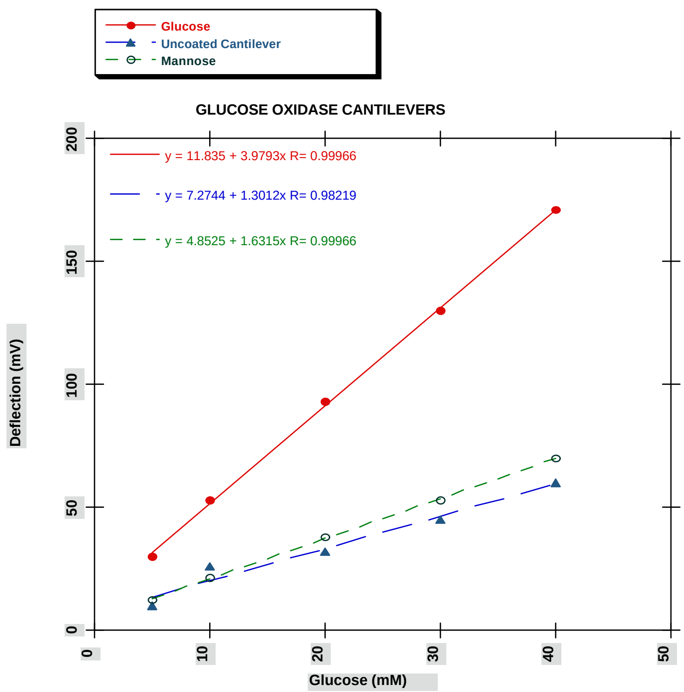

Fig. 2 Data from a calorimetric microcantilever showing cantilever deflection as a function of glucose concentration

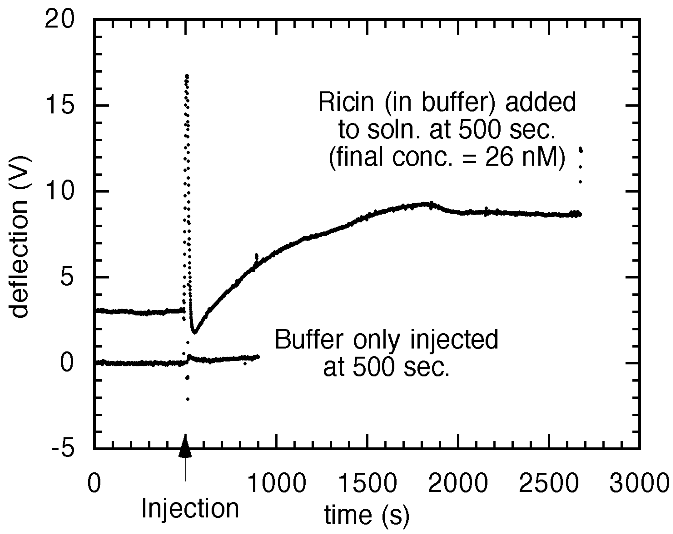

Fig. 3 Chemomechanically induced cantilever deflection by ricin Ag-Ab reaction. The bottom curve shows absence of deflection when Ab-loaded cantilever is exposed to a buffer solution, i.e. without containing ricin Ag.

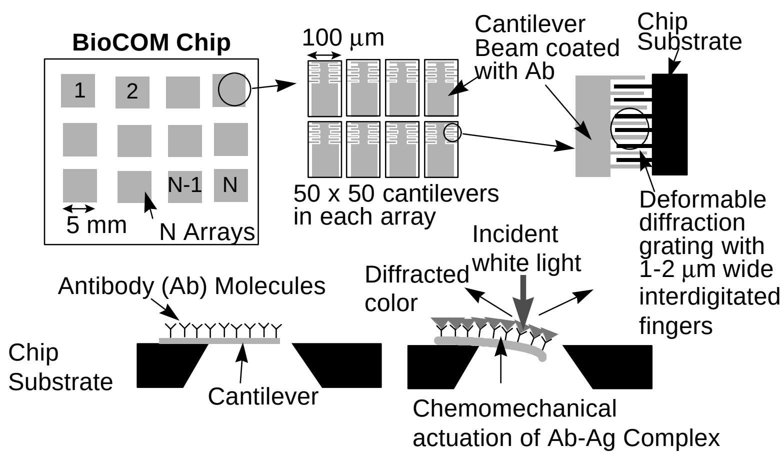

Fig. 4 Design of the BioCOM chip

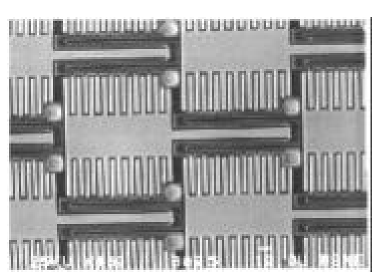

Fig. 5 Electron micrograph of array of microcantilever beams containing enmeshed interdigitated fingers that are used as deformable diffraction gratings for cantilever deflection measurement [8,9].